REMARKS

The Office Action of June 11, 2003, has been received and reviewed. Although the Office Action Summary indicates that the Office Action is Final, per the phone conference with the Examiner, it is noted that the Office Action of June 11, 2003 is a non-final rejection. Claims 1-11, 14-16, 18 and 21-25 are pending in the application and all claims stand rejected. Claims 11 and 15 have been amended as set forth herein. Reconsideration is respectfully requested.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 11, 15-18, 24 and 25 stand rejected under 35 U.S.C. § 112, second paragraph, as assertedly being indefinite. Applicants respectfully traverse the rejections as hereinafter set forth.

Claims 11, 14-18, 24 and 25 were thought to be indefinite "because the steps recited by the methods do not **necessarily** achieve the goal set forth in the claim preamble." (Office Action of June 11, 2003, page 3) (*emphasis added*). Although applicants do not agree that claims 11, 15-18, 24 and 25 are indefinite, to expedite prosecution, claims 11 and 15 have been amended as set forth herein. As amended, claim 11 recites in part "thus screening for the compound that inhibits the binding of the ligand with the extracellular part of the chimeric receptor or with the signaling pathway of the cytoplasmic part of the chimeric receptor" and claim 15 recites in part "thus screening for ligands of an orphan receptor." As amended, claims 11 and 15 indicate that the screening is accomplished.

With further regard to claims 11, 14-18, 24 and 25 , they should be definite since the goal of the preamble does not have to be accomplished. As stated by the Federal Circuit "where the preamble identified the purpose of the claimed invention, the definiteness requirement of 35 U.S.C. § 112 P 2 was met because 'the claimed device [was] **capable** of performing its claimed purpose.'" (*Northern Telecom Limited v. Samsung Electronics Co., LTD.*, 215 F.3d 1281, 1287 n.1, 55 USPQ3d 1065, 1071 n.1 (*Fed. Cir.* 2000), *citing Carl Zeiss Stiftung v. Renishaw pcl*, 945 F.2d 1173, 1181-82, 20 USPQ2d 1094, 1101 (Fed. Cir. 1991) (*emphasis added*)). Thus, the method steps of claims 11, 14-18, 24 and 25 do not **necessarily** have to achieve the goal set forth

in the preamble, but definiteness merely requires that the steps of the method are **capable of** performing the language set forth in the preamble.

It is well known in the art that screening systems may give false positives or negatives, wherein the screening is confirmed by another test. (*See*, Petermann et al., *A recombination based method to rapidly assess specificity of two-hybrid clones in yeast*, Nucleic Acids Res., 1998 May 1, 26(9): 2552-3) (*attached hereto*). Further, patents claiming yeast two-hybrid screening methods, which may result in false positives, have issued. (*See, e.g.*, U.S. Pat. 5,283,173). Thus, claims 11, 15-18, 24 and 25 should be considered definite.

Reconsideration and withdrawal of the indefiniteness rejections of claims 11, 15-18, 24 and 25 are requested.

Rejections under 35 U.S.C. § 103(a)

Claims 1-6, 10, 11, 14-16, 18 and 21-25

Claims 1-6, 10, 11, 14-16, 18 and 21-25 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Pestka et al. in view of Trueheart et al. Applicants respectfully traverse the rejections as hereinafter set forth.

A *prima facie* case of obviousness has not been established with regard to claims 1-6, 10, 11, 14-16, 18 and 21-25 since no suggestion or motivation exists to combine the cited references. Trueheart et al. is limited to the expression of polypeptides from a library to identify polypeptides that agonize or antagonize receptor bioactivity and does not suggest or motivate the use of a chimeric receptor. (*See*, Trueheart et al., page 3). Pestka et al. is limited to a method for identifying or studying a specific ligand and does not suggest or motivate a second recombinant gene, the expression of which creates an autocrinic or anti-autocrinic loop, or a reporter system that is activated or inactivated upon the creation of the autocrinic or anti-autocrinic loop for high throughput screening. (*See*, Pestka et al., page 1).

A *prima facie* case of obviousness also cannot be established since one of ordinary skill in the art would not have a reasonable expectation of success in combining Pestka et al. with Trueheart et al. "In determining the differences between the prior art and the claims, the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious, but

whether the claimed invention as a whole would have been obvious." (M.P.E.P. § 2141.02, *citing Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983) and *Schenck v. Nortron Corp.*, 713 F.2d 782, 218 USPQ 698 (Fed. Cir. 1983) (*emphasis in original*)).

To determine whether one of ordinary skill in the art would combine Pestka et al. with Trueheart et al., the properties of the claimed subject matter as a whole, *i.e.*, the chimeric receptor and the reporter system in the eukaryotic cell, must be considered. Thus, when considering the claimed invention as a whole, one skilled in the art would not expect the chimeric receptor of Pestka et al. to function in the yeast cells of Trueheart et al. Since the receptors of Trueheart et al. are functionally integrated in the signaling pathway, *e.g.*, the endogenous signaling pathway, (*See*, Trueheart et al., page 16, line 26 through page 17, line 1) of the yeast cells of Trueheart et al., the chimeric receptor of Pestka et al. would not be expected to work in the yeast cells of Trueheart et al. without undue experimentation or testing.

Also, one skilled in the art would not expect the autocrinic loops including the G-protein coupled receptors (GPCRs) of Trueheart et al. to function in the cells of Pestka et al. since the cells of Pestka et al. include several hundreds of GPCRs. "One factor which can complicate the use of heterologous expression systems for ligand fishing involves the presence of endogenous receptors in mammalian cell lines and in particular, clonal variation in the pattern of endogenous receptor expression in cells derived from the same parental cell line." (Wilson et al., *Orphan G-protein-coupled receptors: the next generation of drug targets?, British Journal of Pharmacology*, vol. 125, 1387-1392, at p. 1389 (1998)) (previously submitted). Further "the ability to genetically delete endogenous GPCRs from yeast to generate a 'null' background is one of the major advantages in using yeast model systems for orphan receptor screening." (*Id.* at 1390).

Trueheart et al. recognized this problem by reciting "it will be understood to achieve selection or screening, the host cell must have an appropriate phenotype. For example, generating a pheromone-responsive chimeric HIS3 gene in a yeast that has a wild-type HIS3 gene would frustrate genetic selection." (Trueheart et al., page 20). Thus, Trueheart et al. recognizes that the wild-type gene would frustrate genetic selection because of the background

produced by the wild-type gene and, thus, teaches away from combining the teachings of Trueheart et al. with Pestka et al.

Further, the cells of Pestka et al. would be expected to produce a background that may make screening the mammalian cells nearly impossible. As known in the art, mammalian cells include several hundred GPCRs while two GPCRs have been identified in yeast cells. (*See, e.g.*, Versele et al., *Sex and sugar in yeast: two distinct GPCR systems*, EMBO reports, vol. 2, no. 7, 574-579 (2001) (previously submitted). Thus, the background expected from the mammalian cells of Pestka et al. would frustrate selection.

Accordingly, one of skill in the art would not have a reasonable expectation of success in combining Pestka et al. with Trueheart et al. as required to establish a *prima facie* case of obviousness.

Reconsideration and withdrawal of the obviousness rejections of claims 1-6, 10, 11, 14-16, 18 and 21-25 are requested.

Claims 7 and 8

Claims 7 and 8 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Pestka et al. in view of Trueheart et al. as applied to claims 1-6, 10, 11, 14-16, 18 and 21-25, and further in view of Pellegrini et al. Applicants respectfully traverse the rejections as hereinafter set forth.

Claims 7 and 8 are non-obvious, at the very least, as directly or indirectly depending from non-obvious independent claim 1. (*See, In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)). Reconsideration and withdrawal of the obviousness rejections of claims 7 and 8 are, thus, requested.

Claim 9

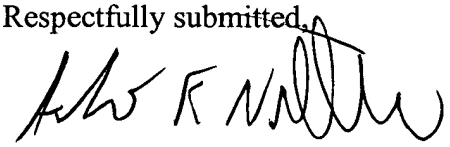
Claim 9 stands rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Pestka et al. in view of Trueheart et al. as applied to claims 1-6, 10, 11, 14-16, 18 and 21-25, and further in view of Mizushima et al. Applicants respectfully traverse the rejections as hereinafter set forth.

Claim 9 is non-obvious, at the very least, as indirectly depending from non-obvious independent claim 1 (*Id.*) Accordingly, reconsideration and withdrawal of the obviousness rejection of claim 9 is requested.

CONCLUSION

In view of the remarks presented herein, applicants respectfully submit that the amended claims define patentable subject matter. If questions should remain after consideration of the foregoing, the Examiner is kindly requested to contact applicants' attorney at the address or telephone number given herein.

Respectfully submitted,



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